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08/876,276	06/16/1997	JAY SHORT	DIVER1280	4852

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EXAMINER

STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/09/2003

4/2

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

08/876,276

Applicant(s)

SHORT ET AL.

Examiner

David J Steadman

Art Unit

1652

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 19-41 and 43-46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 19-41 and 43-46 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Application***

[1] The request filed on July 11, 2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/876,276 is acceptable and a CPA has been established. An action on the CPA follows.

[2] Claims 19-41 and 43-46 are pending.

[3] Applicant's arguments filed in Paper No. 41 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[5] Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 recites the limitation "the prokaryotic cell". There is insufficient antecedent basis for this limitation in the claim. It appears claim 24 should depend from

Art Unit: 1652

claim 22 instead of claim 19 and in the interest of advancing prosecution, claim 24 has been examined accordingly.

***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**[6]** Claims 19-41 and 43-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The examiner can find no support for the limitation of "the bioactivity encoded by the DNA possesses the bioactivity of interest at a temperature at least 10 °C below the temperature of optimal activity of the bioactivity encoded by the wild-type DNA" as recited in claim 41 in the claims, specification, or drawings as originally filed. It is noted that applicant did not specifically point out where such support can be found in the amendment filed June 8, 2000, adding the instant claim.

The examiner can find no support for the limitation of "naturally occurring" as recited in claim 19 (claims 20-41 and 43-46 dependent therefrom) in the claims, specification, and/or drawings as originally filed and there is no description of practicing

Art Unit: 1652

the claimed invention using "naturally occurring DNA". It is noted that applicant did not specifically point out where such support can be found in the amendment filed March 13, 2003 adding the instant limitation.

Applicant is invited to show support for these limitations in the claims, specification, and/or drawings as originally filed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

**[7]** Claims 19, 20, 22, 24-29, 35, 37-39, and 43-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Thompson et al. (US Patent 5,824,485; previously cited in Paper No. 11). Claim 19 is drawn to a method for identifying a bioactivity or biomolecule of interest using high throughput screening of DNA comprising a) contacting a bioactive substrate that is fluorescent in the presence of the bioactivity or biomolecule of interest with a library containing clones containing naturally occurring DNA from more than one organism; b) screening the library with a fluorescent analyzer that detects bioactive fluorescence; and c) identifying clones detected as positive for bioactive fluorescence. Claim 20 is drawn to the method of claim 19 further comprising

Art Unit: 1652

the step of obtaining DNA from a clone that is positive for an enzymatic activity of interest. Claims 22 and 24 limit the library of claim 19 to being generated in a prokaryotic cell or a gram negative prokaryotic cell. Claim 25 limits the clones of claim 19 to being encapsulated in a gel microdrop. Claim 26 is drawn to the method of claim 19, wherein the analyzer screens up to about 15 million clones per hour. Claim 27 limits the clones of claim 19 to extremophiles and claims 28 and 29 further limit the extremophile of claim 27. Claim 35 limits the analyzer to a FACS apparatus. Claim 37 limits the library to an expression library. Claim 38 limits the enzymatic activity to being enhanced relative to a wild-type. Claim 39 is drawn to the method of claim 19, further comprising a step of biopanning (defined in the specification at pages 33-34) the expression library prior to contacting with the substrate. Claim 43 limits the library of claim 19 to a multispecies library and claims 44 and 45 limit the multispecies library of claim 43 to being generated from a mixed population of uncultured organisms or being generated from isolates.

Thompson et al. generally teach methods for generating and screening novel metabolic pathways (see title). Specifically, Thompson et al. teach a method for screening a "combinatorial natural pathway expression library" and detecting an activity, a compound or a gene of interest by, e.g., fluorescence detection by fluorescence-activated cells sorting (FACS) (see, e.g., columns 4-5 and 32-39). A "combinatorial natural pathway expression library" is defined in the disclosure of Thompson et al. as "a library of expression constructs prepared from genetic material derived from a plurality of species of donor organisms, in which genes present in the genetic material are

Art Unit: 1652

operably associated with regulatory regions that drive expression of the genes in an appropriate host organism" (column 6). In particular, Thompson et al. teach "[t]he probe can be an enzyme substrate linked to a fluorogenic agent" (column 36, lines 66-67), which when acted upon by the enzyme, generates a fluorescent product (column 37, top), and provide examples of such (column 36, bottom and column 37, top). Thompson et al. teach the expression library may be pre-screened to increase the number of clones producing the compound of interest, by e.g., hybridization (column 31 bottom – column 32). Thompson et al. teach that the genes identified by the screening method may be isolated for further analysis (column 29, lines 30-36) and are available, e.g., for mutation and further rounds of screening (column 10, lines 13-16). Thompson et al. teach the screened organisms may be prokaryotic including *Escherichia coli* (column 18) and thermophilic, halophilic, acidophilic, barophilic, or methanogenic (column 14, top). Thompson et al. teach the sample may be an organism isolated from an environmental sample that may or may not be cultivated prior to sampling (columns 13 and 14). Thompson et al. teach the library of cells to be screened may be encapsulated into a microdroplet (column 37, lines 55-57). This anticipates claims 19, 20, 22, 24, 25, 27-29, 35, 37, 38, and 43-45 as written.

It is noted that the instant rejection was applied in a previous Office action (see Office action mailed December 07, 1999), was maintained in a subsequent Office action (see Office action mailed October 10, 2000). In the Office action mailed July 20, 2001, the instant rejection is not included and it is unclear as to whether the rejection was intended to be maintained or withdrawn. It is noted that no reasons are provided in the

Art Unit: 1652

Office action mailed July 20, 2001 for withdrawing the instant rejection. In order to clarify the record, upon re-consideration by the examiner, the instant rejection is re-instated.

Applicants' arguments presented in the amendment filed April 16, 2001 are addressed below.

Applicants argue (beginning at page 8) the cited reference does not anticipate the claimed method as Thompson et al. allegedly does not teach preparation of a library of naturally occurring genes in which each clone may contain any type of DNA and wherein the DNA in each clone is obtained from an organism from a mixed population of organisms. Applicant's argument is not found persuasive.

The nucleic acids used to construct the library screened by the method of Thompson et al. clearly encompass naturally occurring DNA obtained from a mixed population of organisms. For example, Thompson et al. describe their library as being "a library of expression constructs prepared from genetic material derived from a plurality of species of donor organisms" and that "[t]he genetic material in each of the host organism encodes naturally-occurring biochemical pathways" (column 6, lines 17-27). At least from this description of their library, one of ordinary skill in the art would recognize the library of Thompson et al. contains clones containing naturally occurring DNA from an organism from a mixed population of organisms.

Applicant argues (pages 9-10) Thompson et al. fails to suggest a method for high-throughput screening of "natural" libraries to identify a bioactivity or biomolecule of interest. Applicant argues Thompson et al. fail to suggest that a library containing a plurality of clones obtained from more than one organism, but wherein each clone



Art Unit: 1652

contains DNA from one organism could be used to discover bioactivities resulting from natural but previously unknown pathways. Applicant's argument is not found persuasive.

It is noted that there is no limitation in the claims that requires that the clones of the library contain "DNA from one organism could be used to discover bioactivities resulting from natural but previously unknown pathways". Nonetheless, Thompson et al. make clear that their library encompasses clones comprising DNA from more than one organism ("a library of expression constructs prepared from genetic material derived from a plurality of species of donor organisms") and teach that "[t]he naturally-occurring pathways of the donor organisms may thus be reconstituted in the host organism" such that "[t]he metabolic pathways of the donor organism may also interact with metabolic pathways resident in the host organism to generate novel compounds or compounds not normally produced by the host organism" (column 5, top).

Applicants argue (at page 11) that Thompson et al. fail to suggest methods useful for causing a fluorescent molecule to enter cells in a library and remain in the cells for a period of time sufficient to conduct high throughput screening of large libraries of molecules. Applicant's argument is not found persuasive.

It would appear that applicant is arguing that the reference of Thompson et al. is not an enabling disclosure, i.e., one of ordinary skill in the art would not be able to practice the method of Thompson et al. using high-throughput screening due to leakage of a fluorogenic substrate. However, it is noted that Thompson et al. clearly state, "[t]he libraries of the invention are compatible with the established multi-well footprint format

Art Unit: 1652

and robotics for high-throughput screening" (column 11, lines 51-54) and "[t]he methods claimed herein enables the management of large sample numbers with minimal handling to permit efficient and high-throughput detection and isolation of productive clones in the library" (column 33, lines 1-4). Thus, the methods of Thompson et al. clearly can be applied to a high-throughput format. Furthermore, as evidenced by Miao et al. (*Biotechnol Bioengineer* 42:708-715), a fluorogenic compound for use with beta-galactosidase with a short staining time was available to one of ordinary skill in the art at the time of the invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**[8]** Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. Claim 23 is drawn to the method of claim 19, wherein the library contains at least about  $2 \times 10^6$  clones.

Thompson et al. disclose the teachings as described above. Thompson et al. do not teach using at least  $2 \times 10^6$  clones to practice their method.

At the time of the invention, one of ordinary skill in the art would have wanted to practice the method of Thompson et al. using at least  $2 \times 10^6$  clones in order to

Art Unit: 1652

increase the likelihood of obtaining a clone expressing an activity of interest. By using at least  $2 \times 10^6$  clones, an ordinarily skilled artisan would have recognized that the statistical probability of identifying a clone comprising an activity of interest would be substantially increased.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to practice the method of Thompson et al. using a library containing at least  $2 \times 10^6$  clones. One would have been motivated to use at least  $2 \times 10^6$  clones in the method of Thompson in order to increase the likelihood of obtaining a clone of interest. One would have a reasonable expectation of success for practicing the method of Thompson et al. using  $2 \times 10^6$  clones because of the results of Thompson et al. and the state of the art. Therefore, claim 23, drawn to a method as described above would have been obvious to one of ordinary skill in the art.

It is noted that the instant rejection was applied in a previous Office action (see Office action mailed December 07, 1999), was maintained in a subsequent Office action (see Office action mailed October 10, 2000). In the Office action mailed July 20, 2001, the instant rejection is not included and it is unclear as to whether the rejection was intended to be maintained or withdrawn. It is noted that no reasons are provided in the Office action mailed July 20, 2001 for withdrawing the instant rejection. In order to clarify the record, upon re-consideration by the examiner, the instant rejection is re-instated. Applicants' arguments presented in the amendment filed April 16, 2001 are addressed below.

Applicants argue (at page 12) that claim 23 depends from claim 19, which is distinguished over Thompson et al. and therefore, Thompson et al. do not anticipate the claim. Applicant's argument is not found persuasive.

As stated above, applicants' arguments do not distinguish the claimed invention over the reference of Thompson et al. Therefore, one of ordinary skill in the art would have wanted to use as many representative clones (at least  $2 \times 10^6$  clones) to practice the method of Thompson et al.,

**[9]** Claims 30-32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. in view of Miao et al. (*Biotechnol Bioengineer* 42:708-715). Claim 30 limits the bioactive substrate of the method of claim 19 to C12FDG. Claim 31 limits the bioactive substrate of the method of claim 19 to comprising a lipophilic tail. Claim 32 is drawn to the method of claim 19, wherein the clones and substrates are heated. Claim 34 limits the heating time of claim 32 to about 30 minutes.

Thompson et al. disclose the teachings as described above. Thompson et al. further teach a method of pre-screening a library containing a beta-galactosidase reporter construct and selecting clones by FACS (column 47). Thompson et al. do not teach using C12FDG as a substrate or a substrate comprising a lipophilic tail. Thompson et al. further do not teach heating the clones and substrates.

Miao et al. teach C12FDG as a fluorogenic substrate for beta-galactosidase. Miao et al. teach C12FDG is an FDG analog with a 12 carbon fatty acid acyl chain added to the 5-position of FDG's fluorescence moiety (page 709, right column, middle). Miao et al. teach a method for screening clones expressing beta-galactosidase using

Art Unit: 1652

C12FDG as a substrate by mixing C12FDG with the cells, heating the cells at 37 degrees Celsius for a few minutes to more than an hour (depending on assay conditions and intracellular beta-galactosidase levels) to allow permeation of the cells (page 709, right column, bottom), and detecting those clones expressing beta-galactosidase by FACS. Miao et al. teach C12FDG overcomes substrate leakage that is a problem with other beta-galactosidase fluorogenic substrates (page 708, right column).

At the time of the invention, it would have been obvious to one of ordinary skill in the art to practice the method of Thompson et al. using a library containing beta-galactosidase as a reporter and C12FDG as a fluorogenic substrate, heating the clones at 37 degrees Celsius for about 30 minutes, and detecting those clones expressing beta-galactosidase by FACS. One would have been motivated to the method of Thompson et al. using a library containing beta-galactosidase as a reporter and C12FDG as a fluorogenic substrate, heating the clones at 37 degrees Celsius for about 30 minutes, and detecting those clones expressing beta-galactosidase by FACS in order to prevent substrate leakage as taught by Miao et al. One would have a reasonable expectation of success for practicing the method of Thompson et al. using C12FDG as a fluorogenic substrate of beta-galactosidase because of the results of Thompson et al. and Miao et al. Therefore, claims 30-32 and 34, drawn to methods as described above would have been obvious to one of ordinary skill in the art.

It is noted that the instant rejection was applied in a previous Office action (see Office action mailed December 07, 1999), was maintained in a subsequent Office action (see Office action mailed October 10, 2000). In the Office action mailed July 20, 2001,

Art Unit: 1652

the instant rejection is not included and it is unclear as to whether the rejection was intended to be maintained or withdrawn. It is noted that no reasons are provided in the Office action mailed July 20, 2001 for withdrawing the instant rejection. In order to clarify the record, upon re-consideration by the examiner, the instant rejection is re-instated. Applicants' arguments presented in the amendment filed April 16, 2001 are addressed below.

Applicant argues (at page 14) the claimed method clearly distinguishes over Thompson et al. and the disclosure of Miao et al. does not overcome the alleged deficiencies of Thompson et al. Applicant argues Miao et al. are silent regarding screening a library containing a plurality of clones obtained from one or more organisms wherein each clone contains DNA from one organism in the multispecies population. Applicant's argument is not found persuasive.

While the reference of Miao et al. alone does not teach the claimed invention, it is the combination of references which clearly would have rendered the invention obvious to one of ordinary skill in the art at the time of the invention.

**[10]** Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. in view of Miao et al. as applied to claims 30-32 and 34 above, and further in view of Hirata et al. (US Patent 4,861,718). Claim 33 is drawn to the method of claim 32, wherein the heating is to a temperature of about 70 degrees Celsius.

Thompson et al. and Miao et al. disclose the teachings as described above. The references of Thompson et al. and Miao et al. do not teach heating the clones at 70 degrees Celsius in the presence of C12FDG.

Hirata et al. teach a nucleic acid encoding a thermostable beta-galactosidase having a temperature optimum at 70 degrees Celsius (see abstract and Figures 3, 4, and 6).

At the time of the invention, it would have been obvious to one of ordinary skill in the art to practice the method of Thompson et al. using a library containing clones comprising the nucleic acid of Hirata et al. encoding a thermostable beta-galactosidase as a reporter and C12FDG as a fluorogenic substrate, heating the clones at 70 degrees Celsius and detecting those clones expressing beta-galactosidase by FACS. One would have been motivated to practice the method of Thompson et al. using a library containing clones expressing the thermostable beta-galactosidase of Hirata et al. and heating the clones at 70 degrees Celsius because screening for clones expressing a desired thermostable enzyme would require a thermostable beta-galactosidase and in this case the thermostable beta-galactosidase of Hirata et al. has optimal enzymatic activity at 70 degrees Celsius, and thus maximum conversion of the fluorogenic substrate would occur at 70 degrees Celsius. One would have a reasonable expectation of success for practicing the method of Thompson et al. using a library containing clones comprising a nucleic acid encoding the thermostable beta-galactosidase of Hirata et al. as a reporter and C12FDG as a fluorogenic substrate, heating the clones at 70 degrees Celsius, and detecting those clones expressing beta-galactosidase by FACS because of the results of Thompson et al., Miao et al., and Hirata et al. Therefore, claim 33, drawn to the method as described above would have been obvious to one of ordinary skill in the art.

Art Unit: 1652

**[11]** Claims 21, 36, 40, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thompson et al. in view of Minshull et al. (US Patent 5,837,458). Claim 21 limits the enzyme of claim 20 to those recited. Claim 36 limits the method of claim 20 to an enzymatic activity of interest that is stable at a temperature of at least about 60 degrees Celsius. Claim 40 is drawn to the method of claim 19 further comprising DNA from an identified clone, mutating a DNA encoding an enzymatic activity of interest and comparing the mutant enzymatic activity to the non-mutant enzymatic activity. Claim 46 is drawn to the method of claim 40, using any of the mutagenesis methods recited in the claim.

Thompson et al. disclose the teachings as described above. Thompson et al. do not teach their method can be used to identify an enzyme of claim 21; an enzymatic activity that is stable at 60 degrees Celsius; altering the nucleotide sequence resulting in a difference in enzymatic activity by any of the methods recited in claim 46.

Minshull et al. generally teach methods of cellular and metabolic engineering by recursive sequence recombination (DNA shuffling). Specifically, Minshull et al. teach using DNA shuffling for modifying thermophilic organisms (column 23) and nucleic acids encoding enzymes (including thermophilic enzymes) such as esterases to improve, e.g., their catalytic rate (columns 24-25 and 28). Minshull et al. teach screening of clones expressing improved enzymes can be screened using FACS (columns 15-16).

Therefore, it would have been obvious to one of ordinary skill in the art to practice the method of Thompson et al. to screen for the enzymes taught by Minshull et al. and optionally to isolate the DNA encoding the desired enzyme and mutate the



Art Unit: 1652

encoding DNA as taught by Minshull et al. One would have been motivated to practice the method of Thompson et al. to screen for the enzymes taught by Minshull et al. and optionally to isolate the DNA encoding the desired enzyme and mutate the encoding DNA in order to alter a property or properties of the encoded enzyme as taught by Minshull et al. One would have a reasonable expectation of success for practicing the method of Thompson et al. to screen for the enzymes taught by Minshull et al. and optionally to isolate the DNA encoding the desired enzyme and mutate the encoding DNA because of the results of Thompson et al. and Minshull et al. Therefore, claims 21, 36, 40, and 46, drawn to the methods as described above would have been obvious to one of ordinary skill in the art.

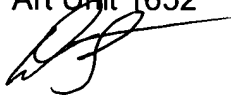
### ***Conclusion***

**[12]** Status of the claims:

- Claims 19-41 and 43-46 are pending.
- Claims 19-41 and 43-46 are rejected.
- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman  
Patent Examiner  
Art Unit 1652

  
**DAVID STEADMAN  
PATENT EXAMINER**